

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 13-22 were pending in this application when last examined and stand rejected.

Claims 13 and 15-22 are cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application on any cancelled subject matter.

Claim 14 is amended to include limitations from claims 17 and 22.

No new matter has been added.

II. ANTICIPATION/OBVIOUSNESS REJECTIONS

In item 6 on pages 3-6 of the Office Action, claims 13-16 and 18-21 were rejected under 35 U.S.C. § 102(b) as being anticipated by Nordisk (WO 98/58646).

It is noted that claim 17 was not subject to this rejection. Claim 14, the only remaining claim, is amended to include the limitation of claim 17. Thus, this rejection is overcome.

Thus, the claimed invention is directed to a method of recovering decreased corneal sensitivity after surgery in a subject with a damaged or cut corneal nerve axon, comprising administering specific SSTR2 or SSTR4 agonist to the subject.

The data of NEI (What is glaucoma?) cited by Examiner never describes that corneal nerve (trigeminal nerve) is damaged in glaucoma. The ophthalmic nerve (optic nerve) and the trigeminal nerve (corneal nerve) are entirely different from each other in the origin of nerve, the destination of sensory nerve, and functions (see **Reference 1**: Foundation of Neurobiology, W.H. Freeman and Company, p.68-71; attached herewith). In particular, the ophthalmic nerve is involved in vision and the destination of this nerve is the lateral geniculate nucleus. In contrast, the function of the trigeminal nerve is to carry sensory input from the face and control muscles that move the jaw and the destination thereof is the mesencephalon pons medulla (see **Reference 1**, pp. 70-71, Table 3-3 and Fig. 3-14, Attachment A).

Thus, as indicated in this reference, even though Nordisk teaches that optic nerve is damaged by glaucoma and SSTR4 agonist can be used for the treatment of glaucoma, Nordisk does not describe that SSTR4 agonist can be used for the recovery of decreased corneal

sensitivity after surgery.

Further, the Examiner finds that Nordisk teaches that Somatostatin can treat inflammation of corneal stroma, stroma keratitis and conjunctivitis; and that such inflammation causes corneal nerve damage as evidenced by Oduntan. However, Oduntan describes that sensory denervation of the conjunctiva elicits an inflammatory response in experimental animals (monkeys), but does not describe that inflammation causes corneal nerve damage. Further, Nordisk does not describe that Somatostatin can be used for the recovery of decreased corneal sensitivity after surgery in a subject with a damaged or cut corneal nerve axon.

Thus, this rejection is untenable and should be withdrawn.

Further, in item 7 on pages 6-8, claims 13-22 were rejected under 35 U.S.C. § 103(a) as obvious over Nordisk (WO 98/58646) in view of Perez-Santonja et al. (AM J. Ophthalmol. 1999, 127:497-504).

Applicants respectfully traverse this rejection as applied to the remaining amended claim.

The Examiner contends that Nordisk does not teach that decreased corneal sensitivity occurs after surgery as recited in instant claim 17, but instead Perez-Santoja teaches that LASIK or PRK can decrease corneal sensitivity. The Examiner therefore concludes that it would have been obvious to one of ordinary skill in the art at the time of the instant invention was made to use somatostatin to treat or recover decreased corneal sensitivity resulting from surgery. Such conclusion necessarily means that the results of treating or recovering decreased corneal sensitivity after surgery by the claimed method would have been expected. Applicants respectfully disagree.

Because Nordisk is not aware that Somatostatin agonist promotes extension of corneal nerve axon, one of ordinary skill in the art would not be motivated to use Somatostatin agonist in a subject with a damaged or cut corneal nerve axon. Perez-Santoja merely describes that LASIK or PRK decreases corneal sensitivity but does not teach that Somatostatin agonist promotes extension of corneal nerve axon. The suggestion for such promotion, and thus motivation to combine these references, comes from this Application. This is impermissible hindsight. Further, one of ordinary skill in the art would not have a reasonable expectation of success in obtaining the claimed invention by combining Nordisk and Perez-Santoja.

Furthermore, the present invention indicates in Experimental Example 5 that use of t-butyl 6-amino-2-(3-(1H-indol-3-yl)-2-((4-(2-oxo-2,3-dihydrobenzimidazol-1-yl)piperidine-1-carbonyl)amino)propionylamino)hexanoate and 1-(3-(N-(5-bromopyridin-2-yl)-N-(3,4-dichlorobenzyl)amino)propyl)-3-(3-(1H-imidazol-4-yl)propyl)thiourea in the claimed method has an unpredictable effect on corneal nerve axon extension. Such unpredictable effect is not taught or suggested in the cited art.

Accordingly, the present invention is not obvious over the combination of Nordisk and Perez-Santoja.

Thus, this rejection, as applied to amended claim 14 is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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